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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,502	07/23/2003	Kyoichi Sumida	14633.1US01	1967

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,502	SUMIDA ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-12,14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 8-12, 14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to the Amendment

The Amendment filed on 07/20/2006 in response to the previous Non-Final Office Action (4/21/2006) is acknowledged and has been entered.

Claims 1, 8-12, 14 and 16 are currently pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 1, 8-12, 14 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Eda et al. (U.S. 6248,597, 2001) and Shigenobu et al. (WO 02/018953, 2002) in further view of Craig et al. (US 4,401,765, 1983).

(Note: All references to the Shigenobou et al. WO publication will be directed to the English translated EP patent application (EP 1314982 A1, 2003).)

Eda et al. teach an agglutination immunoassay of an antigenic analyte comprising performing an antigen-antibody reaction in the presence of a microparticle, wherein the microparticle includes polymeric materials as well as copolymers thereof (column 4, line 67 to column 5, line 5 and column 7, lines 12-19). With regards to the antigenic analyte, the patent teaches (column 5, line 47) that the antigenic analyte may be a tumor marker such as prostate specific antigen (PSA).

Eda et al. does not explicitly teach that the polymer and/or copolymer is represented by the monomer presented in formula [2] and a monomer selected from the group consisting of acrylic acid or acrylate ester, or methacrylic acid or methacrylate ester or styrene. Moreover, Eda et al. does explicitly teach a kit comprising a copolymer obtained by polymerizing a monomer of formula [2] with a second monomer and a prostate specific antibody. Lastly, Eda et al. do not explicitly teach the polymerization of 2-(meth)-acyrloyloxyethyl phosphorylcholine with an aralkyl methacrylate such as benzyl methacrylate

Shigenobu et al. teach a method of improving the reproducibility of an agglutination immunoassay comprising allowing an antigenic substance in a sample to bind to insoluble carrier particles and allowing an antibody or an antibody complex which reacts specifically to the antigenic substance to bind to the antigenic substance in the presence of a polymer (page 2, line 25 and lines 43+). With regards to the insoluble carrier, Shigenobu et al. teach (page 4, lines 24-39) that the insoluble carrier may be latex. With regards to the polymer, the reference teaches (page 5, lines 4-29) that the polymer includes either a polymer having a monomer unit derived from the patently disclosed monomer represented by the general formula [2], wherein the monomer represented by formula [2] is that of 2-methacryloyloxethyl phosphorylcholine (see Sakaki et al. J. Biomedical Materials Research 1999; 47: 523-528 for structure) or a copolymer obtained by polymerizing the monomer represented by 2-methacryloyloxethyl phosphorylcholine with a "second" monomer selected from the group consisting of (meth)acrylates such as acrylate ester, a methacrylate ester, butyl methacrylate or styrene derivatives. Shigenobu et al. further teach (page 5, lines 50-58) that the ratio of the monomer unit derived from 2-methacryloyloxethyl phosphorylcholine in the copolymer is from 1% to 100% and the total polymer molecular weight is 100 to 1,000,000. In addition to the agglutination assay described above, the WO document teaches (page 8, lines 36-47) a reagent kit for an immunoassay comprising combining a reagent containing a copolymer obtained by polymerizing 2-methacryloyloxethyl phosphorylcholine with a monomer as described above, an antibody that binds to the antigen in the sample, and an insoluble carrier protein such as latex, wherein the carrier protein supports the antigen.

Craig et al. teach novel particle reagents for light scattering agglutination immunoassays (Abstract). With regards to the particle reagents, the patent teaches that the particle reagents consist of a core polymer of high refractive index and a shell material which is capable of covalently binding to compounds of biological interest (column 3, lines 35-42). With regards to the core polymers, the patent teaches that polymers with high aromaticity such as benzyl methacrylate are preferred over aliphatic polymers because of their high refractive indices (page 5, lines 1-4 and line 52).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Eda et al. and Shigenobu et al because each of the immunoassays have been individually taught in the prior art to be successful at the detection of antigens. Further, one would have been motivated to do so because as taught by Shigenobu et al., it

is difficult to have a reaction in an agglutination immunoassay, which has good reproducibility due to the non-uniformity of agglutination in an agglutination reaction of the insoluble carrier particles with antigens or antibodies (page 2, lines 19-20). Thus, one of ordinary skill in the art would have a reasonable expectation that by combining the agglutination assay for PSA as taught by Eda et al. with the polymeric material used in the agglutination immunoassay as taught by Shigenobu et al., one would successfully achieve a highly reproducible agglutination immunoassay for prostate specific antigen. Moreover, it would be *prima facie* obvious at the time the invention was made to generate a copolymer obtained by polymerizing 2-methacryloyloxethyl phosphorylcholine with benzyl methacylate instead of the aliphatic methacrylates as taught by Eda et al. and Shigenobu et al. for the use in light scattering agglutination immunoassay in view of the teachings of Craig et al. that polymers with high aromaticity such as benzyl methacrylate are preferred over aliphatic polymers because of their high refractive indices. One would have been motivated to do so because Craig et al. teach that light scattering properties of particle suspensions depend on several variables including the refractive indices, wherein the selection of core material is important in optimizing the sensitivity (column 3, lines 43-51). Thus, one of ordinary skill in the art would have a reasonable expectation that by using a copolymer obtained by polymerizing 2-methacryloyloxethyl phosphorylcholine with benzyl methacylate instead of the aliphatic methacrylates as taught by Eda et al. and Shigenobu et al. in view of the teachings of Craig et al., one would successfully achieve an agglutination immunoassay for prostate specific antigen which has higher sensitivity.

In response to this rejection, Applicants assert that Shigenobu teaches a monomer having a vinyl group that is polymerizable with a monomer having a phosphorylcholine (PC) group. Specifically, Applicants assert Shigenobu discloses monomers having a vinyl group, preferably a n-butyl methacrylate which is different from the methacrylate having the araalkyl group as required by claims 1 and 11. Moreover, Applicants assert that the properties of a product obtained by polymerizing methacrylate lacking the aralkyl group with the monomer of the general formula [2], as disclosed by Shigenobu, are unexpectedly different from the properties of a product obtained by polymerizing an aralkyl methacrylate and the monomer of the general formula [2], as required by claim 1 and 11. As such, Applicants assert that these unexpected results are suggested neither by Eda nor by Shigenobu. Applicants further submit that Craig does not remedy the deficiencies of Eda and Shigenobu. More particularly, Applicants assert that Craig is directed to a particle reagent

consisting of a core polymer having a high refractive index, wherein these core polymers corresponds at best, to the carrier or latex for immobilizing an antibody in the agglutination assay of the present invention, not the agglutination accelerator. Thus, Applicants assert that the rejection assumes that high sensitivity can be achieved by optimizing the refractive index of the agglutination accelerator. However, Applicants assert that the agglutination accelerator itself does not require any light scattering response to obtain superior results in the present invention. In addition, Applicants assert that the reference provides no motivation to use the core polymer as an agglutination accelerator, or to use a copolymer having a benzyl methacrylate and the monomer of the general formula [2] as an agglutination accelerator to obtain the advantageous effects described above or whether poly(benzyl methacrylate) is an appropriate substitute, given that benzyl methacrylate is not used in any of the Examples. Further, Applicants assert that Craig, as well as Eda and Shigenobu fail to suggest any significant differences in effects using a copolymer with different monomers that those employed. As such, Applicants assert that the references actually support the position that the present findings for the copolymers of the monomer of the general formula [2] and aralkyl methacrylate are unexpected.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertion that the properties of the claimed copolymer of the monomer of the general formula [2] and aralkyl methacrylate are unexpected, the Examiner recognizes that objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant (emphasis added). See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence." As such, the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., agglutination accelerator) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re*

Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Regarding Applicants assertion that the "reference", e.g., Craig, provides no motivation, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadlan Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In the instant case, the Examiner recognizes that the motivation to combine the prior art references exists in the nature of the problem to be solved, e.g., a light scattering agglutination immunoassay for PSA with high reproducibility and high sensitivity, wherein Shigenobu et al provides the high reproducibility and Craig provides the sensitivity, in particular incorporation of an arakyl methacrylate such benzyl methacrylate into a copolymer. Thus, Claims 1, 8-12, 14 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Eda et al. (U.S. 6248,597, 2001) and Shigenobu et al. (WO 02/018953, 2002) in further view of Craig et al. (US 4,401,765, 1983).

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
Art Unit 1642

BF
9/20/2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER